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The synthesis of eighteen crown ether compounds with pendant thioamide, *N*-alkylthioamide, and *N,N*-dialkylthioamide groups is reported. The new crown ether compounds are obtained by one-step reactions from the corresponding *sym*-dibenzo-16-crown-5-oxyacetamides and *sym*-(propyl)dibenzo-16-crown-5-oxyacetamides with Lawesson's reagent.

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### Introduction.

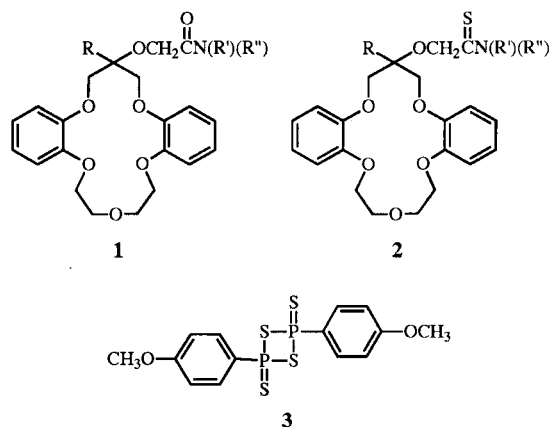
A wide variety of macrocyclic polyether compounds (crown ethers) have been synthesized and utilized for alkali and alkaline earth metal cation separations due to their superior binding abilities for these metal ions [1-3]. When one or more side arms with potential metal ion coordination sites are attached to the crown ether framework, the complexing agents are known as lariat ethers [4]. Such complexing agents may provide three dimensional complexation of metal ions [5].

In recent work, we have prepared dibenzo-16-crown-5 compounds which have pendant functionality attached to the central carbon of the three-carbon bridge [6-9] and studied the behavior of such ionophores towards alkali metal cations in polymeric membrane electrodes [7-9]. Variation of the potential metal ion coordination site in the side arm included ether, ester, and amide groups. The latter were based upon oxyacetate and oxyacetamide 1 units. It was found that attachment of an alkyl group to the same crown ether ring carbon that bears the functional side arm enhanced the sodium ion selectivity of the ion-selective electrodes. The geminal alkyl group orients the functional side arm over the crown ether cavity. It is proposed that such preorganization of the binding site [10] is responsible for the enhancement in sodium selectivity [7-9].

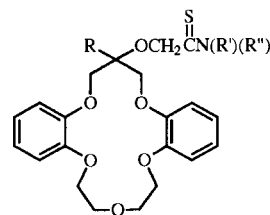
To further probe the effect of functional group variation within the side arm, the synthesis of a series of crown ether thioamides 2 was proposed. If interactions of the metal ion with the side arm are important, incorporation of a soft thioamide donor site would be expected to favor complexation of soft metal ions, such as silver ion, relative to hard alkali metal cations [11]. We now report the synthesis of eighteen dibenzo-16-crown-5 compounds with pendant thioamide, *N*-alkylthioamide, and *N,N*-dialkylthioamide groups.

### Results and Discussion.

The crown ether oxyacetamide precursors 1 were transformed into the corresponding crown ether oxythioacetamides 2 by one-step reactions with Lawesson's reagent (3) as the thionating agent [12-14]. Reaction of *sym*-dibenzo-16-crown-5-oxyacetamides 1 (R = H) with



Lawesson's reagent in toluene gave *sym*-dibenzo-16-crown-5-oxythioacetamides 4-12 in 50-85% yields (Table I). Similar reactions of *sym*-(propyl)dibenzo-16-crown-5-oxyacetamides 1 (R = propyl) provided *sym*-(propyl)dibenzo-16-crown-5-oxythioacetamides 13-21 in 32-69% yields. Except for the case of 1 with R' and R'' = H, the presence of a geminal propyl group in the crown ether oxyacetamide reactant (R = propyl) provided a lower yield than the corresponding compound without a geminal alkyl group (R = H). Structures of the new crown ether thioamides 4-21 were verified by combustion and spectral analysis (Table I).



When R = H	R'	R''	When R = C <sub>3</sub> H <sub>7</sub>
4	H	H	13
5	H	C <sub>3</sub> H <sub>7</sub>	14
6	H	C <sub>5</sub> H <sub>11</sub>	15
7	CH <sub>3</sub>	CH <sub>3</sub>	16
8	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	17
9	C <sub>3</sub> H <sub>7</sub>	C <sub>3</sub> H <sub>7</sub>	18
10	C <sub>4</sub> H <sub>9</sub>	C <sub>4</sub> H <sub>9</sub>	19
11	C <sub>5</sub> H <sub>11</sub>	C <sub>5</sub> H <sub>11</sub>	20
12	C <sub>6</sub> H <sub>13</sub>	C <sub>6</sub> H <sub>13</sub>	21

Table I  
 Yields, Spectral Data and Combustion Analysis Data for Lariat Ether Thioacetamides **4-21**

Compound	mp (°C)	Yield %	<sup>1</sup> H NMR Spectra (200 MHz), ppm [a]	IR Spectrum cm <sup>-1</sup> [b]	Molecular Formula	Combustion Analysis Theory/Found C	H
<b>4</b>	148-149	61	3.91-3.96 (m, 4H), 4.14-4.18 (m, 4H) 4.26 (s, 5H), 4.64 (s, 2H) 6.83-7.05 (m, 8H), 7.68-7.78 (br s, 1 H) 9.20-9.30 (br s, 1H)	3302, 3179 (N-H), 1250, 1120 (C-O)	C <sub>21</sub> H <sub>25</sub> O <sub>6</sub> NS	60.13 60.14	6.01 5.96
<b>5</b>	131-132	74	0.87-0.94 (t, 3H), 1.60 (m, 2H), 3.65 (m, 2H) 3.92 (m, 4H), 4.14-4.24 (m, 9H), 4.65 (s, 2H) 6.86-6.98 (m, 8H), 9.43-9.55 (br s, 1H)	3290 (N-H), 1258, 1112 (C-O)	C <sub>24</sub> H <sub>31</sub> O <sub>6</sub> NS	62.45 62.75	6.77 6.60
<b>6</b>	149-150	72	0.78-0.81 (t, 3H), 1.12-1.38 (m, 4H), 1.52-1.62 (m, 2H), 3.62-3.72 (m, 2H), 3.92-3.94 (m, 4H), 4.14-4.24 (m, 9H) 4.64 (s, 2H), 6.88-6.99 (m, 8H), 9.45-9.55 (br s, 1H)	3275 (N-H), 1248, 1122 (C-O)	C <sub>26</sub> H <sub>35</sub> O <sub>6</sub> NS	63.78 63.65	7.20 7.21
<b>7</b>	102-103	61	3.44 (s, 3H), 3.53 (s, 3H), 3.90-4.00 (m, 4H), 4.10-4.20 (m, 4H), 4.25-4.40 (s, 5H), 4.84 (s, 2H), 6.85-7.00 (m, 8H)	1256, 1124 (C-O)	C <sub>23</sub> H <sub>29</sub> O <sub>6</sub> NS	61.73 61.75	6.53 6.62
<b>8</b>	89-90	80	1.15-1.20 (m, 6H), 3.38 (m, 4H), 3.92-3.94 (m, 4H), 4.14-4.27 (m, 9H), 4.59 (s, 2H), 6.83-6.97 (m, 8H)	1258, 1124 (C-O)	C <sub>25</sub> H <sub>33</sub> O <sub>6</sub> NS	63.14 63.50	7.00 7.20
<b>9</b>	85-86	79	0.89-0.97 (m, 6H), 1.76 (m, 4H), 3.79-3.94 (m, 8H), 4.13-4.17 (m, 4H) 4.31-4.33 (m, 5H), 4.84 (s, 2H) 6.83-6.99 (m, 8H)	1259, 1124 (C-O)	C <sub>27</sub> H <sub>37</sub> O <sub>6</sub> NS	64.39 64.43	7.40 7.50
<b>10</b>	83-84	79	0.89-0.97 (m, 6H), 1.34-1.37 (m, 4H), 1.65-1.70 (m, 4H), 3.82-3.95 (m, 8H), 4.13-4.17 (m, 4H), 4.30-4.33 (m, 5H), 4.83 (s, 2H), 6.82-6.98 (m, 8H)	1258, 1124 (C-O)	C <sub>29</sub> H <sub>41</sub> O <sub>6</sub> NS	65.51 65.77	7.77 7.90
<b>11</b>	63-64	85	0.87-0.93 (m, 6H), 1.30-1.33 (m, 8H), 1.69-1.73 (m, 4H), 3.81-3.95 (m, 8H), 4.13-4.17 (m, 4H), 4.30-4.33 (m, 5H), 4.83 (s, 2H), 6.83-7.00 (m, 8H)	1258, 1124 (C-O)	C <sub>31</sub> H <sub>45</sub> O <sub>6</sub> NS	66.52 66.65	8.10 8.11
<b>12</b>	38-39	50	0.85-0.91 (m, 6H), 1.28-1.30 (m, 12H), 1.61-1.68 (m, 4H), 3.81-3.95 (m, 8H), 4.13-4.17 (m, 4H), 4.30-4.33 (m, 5H), 4.83 (s, 2H), 6.83-6.98 (m, 8H)	1258, 1124 (C-O)	C <sub>33</sub> H <sub>49</sub> O <sub>6</sub> NS	67.43 67.59	8.40 8.33
<b>13</b>	65-67	69	1.01-1.08 (t, 3H), 1.45-1.57 (m, 2H), 1.88-1.96 (m, 2H), 3.84-3.98 (m, 4H), 4.13-4.17 (m, 6H), 4.53-4.58 (d, 2H), 4.96 (s, 2H), 6.81-6.98 (m, 8H), 7.55-7.66 (br s, 1H), 8.64-8.75 (br s, 1H)	3414, 3304 (N-H), 1257, 1122 (C-O)	C <sub>24</sub> H <sub>31</sub> O <sub>6</sub> NS	62.45 62.53	6.77 6.71
<b>14</b>	144-145	64	0.85-0.92 (t, 3H), 1.01-1.08 (t, 3H), 1.51-1.59 (m, 4H), 1.98-2.01 (m, 2H), 3.59-3.63 (m, 2H), 3.80-4.25 (m, 10H), 4.52-4.57 (d, 2H), 4.97 (s, 2H), 6.80-6.95 (m, 8H), 8.80-9.02 (br s, 1H)	3329 (N-H), 1257, 1122 (C-O)	C <sub>27</sub> H <sub>37</sub> O <sub>6</sub> NS	64.39 64.30	7.40 7.78
<b>15</b>	114-115	49	0.79-0.82 (t, 3H), 1.01-1.08 (t, 3H), 1.21-1.24 (m, 4H), 1.49-1.53 (m, 4H), 1.88-2.00 (m, 2H), 3.64-3.70 (m, 2H), 3.87-4.18 (m, 10H), 4.53-4.58 (d, 2H), 4.97 (s, 2H), 6.80-6.93 (m, 8H), 8.89-9.01 (br s, 1H)	3330 (N-H), 1257, 1122 (C-O)	C <sub>29</sub> H <sub>41</sub> O <sub>6</sub> NS• 0.1 H <sub>2</sub> O	65.29 65.04	7.78 7.78
<b>16</b>	122-123	56	0.97-1.04 (t, 3H), 1.45-1.56 (m, 2H), 1.89-1.99 (m, 2H), 3.36 (s, 3H), 3.50 (s, 3H), 3.90-3.94 (m, 4H), 4.12-4.22 (m, 6H), 4.34-4.39 (d, 2H), 4.95 (s, 2H), 6.80-6.94 (m, 8H)	1257, 1122 (C-O)	C <sub>26</sub> H <sub>25</sub> O <sub>6</sub> NS	63.78 64.02	7.20 7.35
<b>17</b>	oil	61	0.96-1.04 (t, 3H), 1.21-1.31 (m, 6H), 1.49-1.59 (m, 2H), 1.88-1.98 (m, 2H), 3.78-3.97 (m, 8H), 4.13-4.23 (m, 6H), 4.33-4.38 (d, 2H), 4.92 (s, 2H), 6.80-6.95 (m, 8H)	1256, 1122 (C-O)	C <sub>28</sub> H <sub>39</sub> O <sub>6</sub> NS	64.96 65.21	7.59 7.42

Table I (continued)

Compound	mp (°C)	Yield %	<sup>1</sup> H NMR Spectra (200 MHz), ppm [a]	IR Spectrum cm <sup>-1</sup> [b]	Molecular Formula	Combustion Analysis	
						Theory/Found C	H
18	123-124	52	0.82-1.03 (m, 9H), 1.48-1.58 (m, 2H), 1.66-1.77 (m, 4H), 1.90-1.98 (m, 2H), 3.68-3.95 (m, 8H), 4.13-4.21 (m, 6H), 4.34-4.39 (d, 2H), 4.96 (s, 2H), 6.80-6.96 (m, 8H)	1257, 1122 (C-O)	C <sub>30</sub> H <sub>43</sub> O <sub>6</sub> NS	66.03 66.08	7.94 8.11
19	102-103	47	0.81-1.03 (m, 9H), 1.24-1.36 (m, 4H), 1.57-1.69 (m, 6H), 1.90-1.95 (m, 2H), 3.75-3.95 (m, 8H), 4.13-4.21 (m, 6H), 4.34-4.39 (d, 2H), 4.96 (s, 2H), 6.81-6.94 (m, 8H)	1225, 1122 (C-O)	C <sub>32</sub> H <sub>47</sub> O <sub>6</sub> NS	66.98 67.04	8.26 8.19
20	oil	33	0.76-1.03 (m, 9H), 1.20-1.32 (m, 8H), 1.42-1.80 (m, 6H), 1.91-2.01 (m, 2H), 3.75-3.93 (m, 8H), 4.13-4.20 (m, 6H), 4.35-4.40 (d, 2H), 4.96 (s, 2H), 6.80-6.94 (m, 8H)	1257, 1122 (C-O)	C <sub>34</sub> H <sub>51</sub> O <sub>6</sub> NS	67.85 67.59	8.54 8.25
21	oil	32	0.81-1.02 (m, 9H), 1.10-1.32 (m, 12H), 1.36-1.75 (m, 6H), 1.88-1.98 (m, 2H), 3.79-3.95 (m, 8H), 4.12-4.19 (m, 6H), 4.35-4.49 (d, 2H), 4.96 (s, 2H), 6.79-6.94 (m, 8H)	1257, 1122 (C-O)	C <sub>36</sub> H <sub>55</sub> O <sub>6</sub> NS	68.65 69.05	8.80 8.75

[a] In deuteriochloroform. [b] Deposit from dichloromethane solution on a sodium chloride plate.

Compounds **4-21** represent a series of crown ether thioamides with systematic structural variation. For **4** and **13**, the sidearm is oxythioacetamide. In **5**, **6**, **14**, and **15**, the side arm is *N*-alkoxythioacetamide with propyl and pentyl alkyl groups. Compounds **7-12** and **16-21** have *N,N*-dialkyl oxythioacetamide groups in which the alkyl groups are varied from methyl to ethyl to propyl to butyl to pentyl to hexyl. For **13-21**, the presence of the geminal propyl group is expected to orient the thioacetamide group in the side arm over the crown ether cavity; whereas for the analogous compounds **4-12**, greater conformational flexibility of the side arm is anticipated.

Although the ir spectral absorption for the carbonyl group of the amide function in **1** disappeared when it was converted into the corresponding thioamide compound **2**, no new band for the thiocarbonyl group could be discerned. This is consistent with literature reports of strong vibrational coupling effects in infrared spectra of thioamides and the absence of a localized C=S vibration [15,16]. In the ir spectra of acetamides **4** and **13** (Table I), two N-H stretching vibrations are noted at 3302, 3179 and 3414, 3304 reciprocal centimeters, respectively, for conformations with C=S *cis* and *trans* to the N-H bond. On the other hand for the *N*-alkylacetamides **5**, **6**, **14**, and **15**, there are single absorption bands at 3,290, 3,275, 3,329 and 3,330 reciprocal centimeters, respectively, for the N-H stretching vibration. In their <sup>1</sup>H nmr spectra, acetamides **4** and **13** exhibit two broad singlets for *cis* and *trans* arrangements of the N-H bond with respect to the C=S bond. For *N*-alkylacetamides **5**, **6**, **14**, and **15** only one

broadened singlet is observed.

The metal ion complexing abilities of crown ether thioacetamides **4-21** have been evaluated by metal picrate extraction and by transport of metal perchlorates across bulk chloroform membranes [17]. In these investigations, the new ligands have been found to exhibit a high propensity for complexation of silver ion relative to the alkali metal cations. The results of that study will be reported separately.

## EXPERIMENTAL

The ir spectra were obtained with a Perkin Elmer Model 1600 spectrophotometer and are reported in reciprocal centimeters. The <sup>1</sup>H nmr spectra were recorded with an IBM AF-200 spectrometer in deuteriochloroform and chemical shifts are reported in parts per million (δ) from TMS. Combustion analysis was performed by Desert Analytics (Tucson, Arizona).

Unless specified otherwise, reagent grade reactants and solvents were used as received from commercial suppliers. Toluene was stored over activated 4 Å molecular sieves under nitrogen. The *sym*-(*R*)dibenzo-16-crown-5-oxyacetamides were prepared by the reported method [6].

Preparation of *sym*-Dibenzo-16-crown-5-oxyacetamide (**4**).

The following procedure is representative of that by which crown ether oxythioamides **5-21** were prepared.

A mixture of *sym*-dibenzo-16-crown-5-oxyacetamide (4.39 g, 10.88 mmoles) and Lawesson's reagent (2.20 g, 5.44 mmoles) in 250 ml of toluene was refluxed for 10 hours. The reaction mixture was allowed to cool to room temperature and the solvent was evaporated *in vacuo*. The residue was dissolved in dichloro-

methane (300 ml) and the solution was washed with water (2 x 150 ml), dried over magnesium sulfate and evaporated *in vacuo* to give a brownish oil. The oil was chromatographed on silica gel with dichloromethane then ethyl acetate as eluents to give a colorless oil which was crystallized from 50 ml of diethyl ether to give 2.77 g (61%) of **4** as a white solid.

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